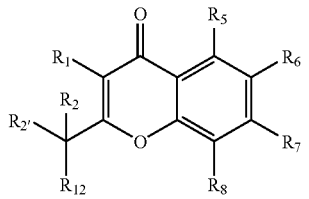
fragments and variants thereof. The inhibition can be of the ATP hydrolysis activity of the KSP kinesin and/or the mitotic spindle formation activity, such that the mitotic spindles are disrupted. Meiotic spindles may also be disrupted.

[0095] An object of the present invention is to develop inhibitors of mitotic kinesins, in particular KSP and especially human KSP, for the treatment of disorders associated with cell proliferation. Traditionally, dramatic improvements in the treatment of cancer, one type of cellular proliferative disorder, have been associated with identification of therapeutic agents acting through novel mechanisms. Examples of this include not only the taxane class of agents that appear to act on microtubule formation, but also the camptothecin class of topoisomerase I inhibitors. The compounds, compositions and methods described herein can differ in their selectivity and are preferably used to treat diseases of cellular proliferation, including, but not limited to cancer, hyperplasias, restenosis, cardiac hypertrophy, immune disorders, fungal disorders and inflammation.

[0096] Accordingly, the present invention relates to methods employing compounds represented by Formula I:

Formula I



wherein:

[0097] R_1 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

[0098] R_2 and $R_{2'}$ are independently chosen from hydrogen, optionally substituted alkyl-, optionally substituted alkoxy, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-; or R_2 and $R_{2'}$ taken together form an optionally substituted 3- to 7-membered ring;

[0099] R_{12} is selected from the group consisting of optionally substituted imidazolyl, optionally substituted imidazolinyl, —NHR_4; —$N(R_4)(COR_3)$; —$N(R_4)(SO_2R_{3a})$; and —$N(R_4)(CH_2R_{3b})$;

[0100] R_3 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, $R_{15}O$— and R_{17}—NH—;

[0101] R_{3a} is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, optionally substituted heteroaralkyl-, and R_{17}—NH—;

[0102] R_{3b} is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-;

[0103] R_4 is chosen from hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heterocyclyl-, and optionally substituted heteroaralkyl-;

[0104] R_5, R_6, R_7 and R_8 are independently chosen from hydrogen, acyl, optionally substituted alkyl-, optionally substituted alkoxy, halogen, hydroxyl, nitro, cyano, dialkylamino, alkylsulfonyl-, alkylsulfonamido-, alkylthio-, carboxyalkyl-, carboxamido-, aminocarbonyl-, optionally substituted aryl and optionally substituted heteroaryl-;

[0105] R_{15} is chosen from optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, and optionally substituted heteroaralkyl-, and

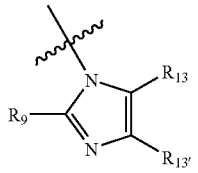
[0106] R_{17} is hydrogen, optionally substituted alkyl-, optionally substituted aryl-, optionally substituted aralkyl-, optionally substituted heteroaryl-, or optionally substituted heteroaralkyl-, including single stereoisomers, mixtures of stereoisomers;

[0107] a pharmaceutically acceptable salt of a compound of Formula I;

[0108] a pharmaceutically acceptable solvate of a pharmaceutically acceptable solvate of a compound of Formula I;

[0109] or a pharmaceutically acceptable solvate of a pharmaceutically acceptable salt of a compound of Formula I.

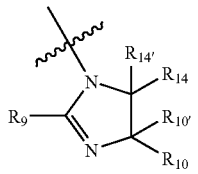
[0110] When R_{12} is an imidazole, R_{12} has the formula:



wherein

[0111] R_9 is chosen from hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted aryl, optionally substituted aryl-C_1-C_4-alkyl-, optionally substituted heteroaryl-C_1-C_4-alkyl-, optionally substituted aryl-C_1-C_4-alkoxy-, optionally substituted heteroaryl-C_1-C_4-alkoxy-, optionally substituted heteroaryl-; and R_{13} and $R_{13'}$ are independently hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted aryl, or optionally substituted aryl-C_1-C_4-alkyl-.

[0112] When R_{12} is an imidazoline, R_{12} has the formula



wherein

[0113] R_9 is chosen from hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted aryl, optionally substituted aryl-C_1-C_4-alkyl-, and optionally substituted heteroaryl-; and R_{10}, $R_{10'}$, R_{14}, and $R_{14'}$ are independently chosen from hydrogen, optionally substituted C_1-C_8 alkyl, optionally substituted aryl, and optionally substituted aryl-C_1-C_4-alkyl-.

[0114] In one embodiment, R_1 is chosen from hydrogen, optionally substituted alkyl, optionally substituted aryl, optionally substituted aralkyl, optionally substituted heteroaryl, and optionally substituted heteroaralkyl-;